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Introduction

The physiological fluid movement through a vascular membrane into the surrounding tissue depends on the 3 factors membrane permeability, oncotic pressure gradient and hydrostatic pressure gradient. As additional factor lymphatic drainage counteracts extravascular fluid accumulation. *Oedema* develops, if one of these 4 factors is disturbed in a degree that cannot be compensated. For *pulmonary oedema* to develop, essentially always an increased intravascular hydrostatic pressure or a disturbed vascular permeability is responsible. For clinical purposes, pulmonary oedema is grossly divided based on pathophysiology in cardiogenic and non-cardiogenic oedema. The exact differentiation and diagnosis is made based on a combination of clinical and radiological findings and considerations.

Pathogenesis and causes of cardiogenic pulmonary oedema

Cardiogenic pulmonary oedema develops secondary to a rise of hydrostatic pressure in the pulmonary capillaries (normal <12 mmHg). When rise in pressure is gradual, pressure may exceed 20 mmHg before pulmonary oedema develops, because the capacity of lymphatic drainage can be increased. For cardiogenic pulmonary oedema to develop, by definition there must be left-sided congestive heart failure for which there must be an identifiable underlying cardiac disease. Most important diseases are acquired, advanced degenerative mitral valve disease and dilated cardiomyopathy, and congenital, patent ductus arteriosus.
Radiologically, congestion is manifested by dilated pulmonary veins and cardiogenic oedema that in dogs initially is characterized by an increased interstitial lung pattern progressing to an alveolar pattern. Typically, the oedema starts in the perihilar area progressing to the caudo-dorsal lung parts. In addition, there should generally be clear radiological signs of left sided cardiac disease with distinct left atrial dilation as well as clear clinical signs of an underlying cardiac disease that concurs with the radiograph findings.

Pathogenesis and causes of non-cardiogenic pulmonary oedema

Various mechanisms are responsible for non-cardiogenic oedema to develop, i.e. low alveolar pressure, increased vascular permeability, increased hydrostatic pressure and a combination of these. The various causes, according to pathophysiology are: low alveolar pressure – post obstructive oedema; low alveolar pressure – re-expansion oedema; neurogenic oedema; vasculitis; high altitude pulmonary oedema.

Decreased alveolar pressure develops after fast removal of pleural effusion, pneumothorax, or lung lobes, called re-expansion oedema. Mortality of this rare complication in people is described as 20%. In veterinary medicine, 2 feline cases have been described that both died. Decreased alveolar pressure also results from upper airway obstruction, called post obstructive oedema; e.g. in brachycephalic syndrome, laryngeal paralysis, tracheal collapse, strangulation, and iatrogenic during intubation and bronchoscopy. The non-cardiogenic oedema in some hunting dogs may partially be caused by obstruction, specifically laryngeal oedema associated with prolonged and constant barking. More likely in these dogs is a neurogenic oedema associated with a very high catecholamine level (see below). Post obstructive pulmonary oedema in dogs and cats is probably much more common than diagnosed. Many cases are probably diagnosed as cardiogenic oedema, because dyspnoea and oedema are associated with exercise or a stress situation, e.g. in laryngeal paralysis or oedema associated with anaesthesia, or because affected animals may have two concomitant disease, e.g. tracheal collapse and degenerative mitral valve disease.

A further important cause of non-cardiogenic oedema is neurogenic oedema. Pathophysiologically, excessive sympatho-adrenergic activation in the medulla oblongata plays the central role. This results in pulmonary venous constriction shifting blood from the systemic to the pulmonic circulation, increase in pulmonary hydrostatic pressure and finally oedema. Causes described in dogs are brain trauma, epileptic seizures and electrocution. The pulmonary oedema in hunting dogs during or after the hunt is also thought to be caused by excessive catecholamine secretion, and thus to be a neurogenic oedema. A particular pathogenesis of neurogenic pulmonary oedema is the one in endurance athletes caused by cerebral oedema elicited by hyponatraemia. Prognosis for complete recovery in neurogenic oedema is good with adequate supportive care.

Of big importance for the development of non-cardiogenic oedema is the acute (formerly adult) respiratory distress syndrome, ARDS. The underlying cause is severe and diffuse damage of the lung parenchyma resulting in endothelial and epithelial disturbance of permeability and exit of protein rich fluid. Complicating factors are coagulation disturbances, perfusion disturbances and loss of surfactant. ARDS may be a complication of primary lung damage, e.g. after inhalation of toxic gas (smoke intoxication), aspiration of gastric content, inhalation of hyperbaric oxygen (oxygen intoxication) or pneumonia. ARDS may also be a complication of a severe systemic disease like sepsis, extensive burn and acute pancreatitis. The prognosis even with intensive supportive care is poor. Pulmonary oedema similar to ARDS can be elicited by multiple blood transfusions; even though this complication is life threatening, the prognosis is much better than in ARDS.

A further important cause of protein-rich pulmonary oedema is vasculitis and disturbed vascular permeability, in dogs well recognized in leptospirosis. This may be complicated by prognostically important pulmonary haemorrhages that may not be differentiated radiologically from oedema.
Finally, high altitude above around 3000 m may cause non-cardiogenic pulmonary oedema in susceptible individuals.

No pulmonary oedema in low oncotic pressure

Even though oncotic pressure, primarily depending on plasma albumin concentration, is one of the important factors to keep fluid inside the vasculature, it does not play an important role in the lungs. The pulmonary interstitial space normally has a higher albumin concentration than other interstitial tissue and a small oncotic gradient, because the permeability of pulmonary capillaries is higher than in other capillaries. When plasma albumin drops, the interstitial albumin concentration drops as well, therefore not markedly affecting the oncotic gradient. Thus, it is unusual to find pulmonary oedema when hypoalbuminaemia is the only abnormality.

Therapeutic principles for pulmonary oedema

In cardiogenic pulmonary oedema the central therapeutic focus is to decrease preload by aggressive diuresis using loop diuretics. In contrast, the various mechanisms of non-cardiogenic oedema are not affected by diuresis. Even more, in various diseases fluid therapy rather than diuresis to supportively treat the underlying disease is indicated, e.g. in sepsis, pancreatitis and leptospirosis. However, in these cases, infusion therapy has to be defensive / cautious. The primary supportive measure is optimized oxygenation. Depending on oedema cause and severity keeping an animal quiet in an oxygen-rich environment may suffice, or artificial respiration using positive endexspiratory pressure (PEEP) may be needed. The usefulness of glucocorticoids is controversial. In a recent human study, low dose and early application of methylprednisolone had a positive effect on the course in ARDS. Furthermore, extrapolated from human medicine, steroids seem useful in the pulmonary oedema in leptospirosis.

In summary, cardiogenic and non-cardiogenic causes are responsible for pulmonary oedema to develop. The exact identification of the underlying cause is of paramount importance for therapy and prognosis. With progressive specialisation also in intensive care medicine and with similar large dedication of veterinarians and animal owners for time-consuming and costly treatments, more and more so-called hopeless cases may be completely cured.

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